Other Manufacturing Functions: Recovery, Storage, Labeling

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CENTER FOR BIOLOGICS EVALUATION AND RESEARCH

Other Manufacturing Functions

- *Recovery*
- *Labeling Controls*
- *Storage*
- *Labeling*

Recovery
21 CFR 1271.3(ii)

Obtaining from a human donor cells or tissues that are intended for use in human implantation, transplantation, infusion, or transfer.

Recovery
21 CFR 1271.215

If you are an establishment that recovers HCT/Ps, you must recover each HCT/P in a way that does not cause contamination or cross-contamination during recovery, or otherwise increase the risk of the introduction, transmission, or spread of communicable disease through the use of the HCT/P

Recovery
21 CFR 1271.215
(Continued)

- You must establish and maintain procedures for cell and tissue recovery.
- [No comments were received on this provision]

Labeling Controls
21 CFR 1271.250

a. General
   - Establish and maintain procedures to control the labeling of HCT/Ps.
   - Design procedures to ensure proper HCT/P identification and to prevent mix-ups

Labeling Controls
21 CFR 1271.250

b. Verification

– Procedures must include verification of label accuracy, legibility, and integrity.

Labeling Controls
21 CFR 1271.250

c. Labeling Requirements

Procedures must ensure that each HCT/P is labeled in accordance with all applicable labeling requirements, including those in

- 1271.55 Records that accompany; records to be retained
- 1271.60 Requirements that apply before DE determination
- 1271.65 Storage of HCT/P from ineligible donor
- 1271.90 Exceptions from DE and labeling requirements
- 1271.290 Facilities
- 1271.370 Labeling

Labeling Controls
21 CFR 1271.250

c. (continued)

Procedures must ensure that each HCT/P made available for distribution is accompanied by documentation of the donor eligibility determination as required under under 1271.55

Labeling Controls
21 CFR 1271.250

[Comments 104 & 105]

- Comments asserted these requirements as applied to in-house distribution are too burdensome
- Asserted the type of info is exorbitant for the ID of individual products
- FDA disagreed; believing it is important for the physician to have accurate, specific info
- However, FDA modified 21 CFR 1271.55 to mod the records requirement

Storage
21 CFR 1271.3(jj)

Storage means holding HCT/Ps for future processing and/or distribution.

Storage
21 CFR 1271.260

a. Control Storage areas to prevent,

(1) Mix-ups, contamination, and cross-contamination of HCT/Ps, supplies and reagents

(2) An HCT/P from being improperly made available for distribution

b. Temperature. You must store HCT/Ps at an appropriate temperature

Storage
21 CFR 1271.260
[Comment 106]

- Asked whether establishments must validate storage temp and period requirements in PR.
- Noted many have been established by the industry based on experience
- FDA agrees establishments may follow industry std where the std meet regulatory requirements
- Industry may establish and validate their own criteria

Storage
21 CFR 1271.260

c. Expiration date. *Where appropriate*, you must assign an exp date based on the following factors:

1. HCT/P Type

2. Processing,- incl. method of preservation

3. Storage conditions

4. Packaging

Storage
21 CFR 1271.260

d. Corrective Action.

   You must take and document corrective action whenever proper storage conditions are not met.

Storage
21 CFR 1271.260
[Comment 107]

- Two comments stated the safe duration of cryopreservation for hematopoietic stem/prog cells is unknown and will take years to validate

- FDA discusses exp date for “fresh” HCT/Ps, and those thawed after cryopreservation;
- If no scientific data exist, then no exp date is required at this time;
- FDA encourages further studies

Storage
21 CFR 1271.260

e. Acceptable temperature limits. You must:

- Establish acceptable temperature limits for storage for each step of mfr. to inhibit growth of infectious agents
- Maintain and record temperatures
- Periodically review recorded temps

Subpart E
Additional Requirements
Labeling
21 CFR 1271.370

Subpart E -Additional Requirements Labeling 21 CFR 1271.370

Apply in addition to to 1271.55,1271.60, 1271.65 and 1271.90

- a. HCT/P made available for distribution must be labeled clearly and accurately.

Subpart E -Additional Requirements Labeling 21 CFR 1271.370

b. Following information must appear on the HCT/P label:

1. Distinct ID code affixed to HCT/P container and assigned in accordance with 1271.290(c) [Tracking]
2. Description and type of HCT/P
3. Expiration date, if any
4. Warnings required under 1271.60(d)(2),1271.65(b)(2) or 1270.90(b), if applicable

“Label”
[Comment 146]

- The term “label” in this subpart means either:
  1. Affix to the HCT/P container, or
  2. Attach a tie-tag with the appropriate info to the container

Additional Requirements Labeling 21 CFR 1271.370 [Comment 147]

- One comment stated that guidance is needed on “warnings”
- In response, FDA added 1271.370(b)(4), which lists as information the warnings required under 1271.60, 1271.65, or 1271.90, as applicable
- Pertaining to communicable disease risks

Additional Requirements Labeling 21 CFR 1271.370 [Comment 147]

- FDA now requires warning statements related to informing the recipient about certain unusual circumstances
- e.g. “WARNING: Advise patient of communicable disease risk” when HCT/P is distributed before completion of DE determination

Subpart E -Additional Requirements Labeling

21 CFR 1271.370

c. Information must appear on the HCT/P label or *accompany* the HCT/P:

1. Name and address of establishment that makes release determin. and makes HCT/P available for distrib.
2. Storage temperature
3. Other warnings, *where appropriate*
4. Instructions for use when related to the prevention, introduction, transmission or spread of comm. diseases

Additional Requirements
Labeling
21 CFR 1271.370

- See Comments 149, 150, 151
- FDA has removed “claims” provision from 1271.370
- FDA has added the terms “repair” and “reconstruction” to the definition of “homologous use” at 1271.3c.